and passes meconium and voids urine normally. Mucus in the throat and nasopharynx is unusually profuse in amount. Liquid is taken hungrily, but is regurgitated within a few minutes, often with cyanosis and coughing. The vomitus contains much mucus and is foamy in appearance.

With the advent of roentgenologic observation it was possible to confirm the diagnosis by obstruction to the passage of the esophageal catheter and later by outlining the sac with bismuth or barium. In our patients lipiodol gave an accurate estimate of the size and character of the malformation. The use of iodized oil in the examination has the advantages of accuracy in filling of possible tiny fistulous tracts, of ease of administration and relative safety for the respiratory tract, since we may expect aspiration into the bronchial tree. Should the esophagus prove patent the oil is harmless in the stomach.

No cases of surgical cure of atresia of the esophagus are on record. Remedial measures must be aimed at correcting the communication with the bronchial tree as well as providing nourishment or the infant will die of pulmonary infection.

Although the diagnosis of congenital atresia of the esophagus is not difficult, it is one with a hopeless prognosis. Clear-cut visualization of the defect gives assurance to the physician in explaining the situation to the distressed family of the infant.

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I wish to express appreciation to Dr. C. E. von Geldern for his interest and care in making the drawing of the necropsy specimen of Case 1.—R. S. G.

THE DIAGNOSIS OF MALIGNANCY BY THE STUDY OF THE CENTRIFUGED SEDIMENT OF ASCITIC AND PLEURAL FLUIDS*

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THE technique of centrifuging ascitic and pleural fluids with the expectation of finding and recognizing tumor cells in the sediment is not new. The value of these examinations lies in the fact that they afford an additional source of information in cases that often are not well defined clinically. Frequently a tentative clinical diagnosis of malignancy is confirmed, and occasionally a definite diagnosis of malignancy is made in cases that, clinically, appeared to be nonmalignant. The examination of a pleural fluid may give one of the first clues to the presence of an intrathoracic malignancy. Ascitic fluids from patients with obscure abdominal conditions may contain numerous malignant cells and thus obviate an exploratory operation. These examinations lack, however, the clinical popularity they should have. This is due in part to the use of indifferent methods in the preparation of the sediment and in part to difficulty in the interpretation of the microscopic pictures obtained.

METHODS IN USE

Two methods of examining the centrifuged sediment are in common use. The simpler, and the less satisfactory, is to smear part of the sediment on a slide and treat it as an ordinary blood smear. The staining qualities of the cells so treated are usually quite indifferent and the average slide gives a blurred picture worth relatively little for diagnostic purposes. With good technique and fresh fluids, well-stained slides are obtainable, but even with these the interpretation of the less common cell types is frequently difficult and uncertain.

The second method, that of embedding and sectioning the sediment, is more time-consuming, but when properly done gives excellent results. The technique employed during the preparation of the centrifuged sediment is of extreme importance, as the success or failure of the method depends almost entirely upon the physical properties of the sediment. A nonfriable, firm sediment which can be handled as roughly as an ordinary block of tissue is necessary for satisfactory study. Such a sediment rarely can be obtained from fluids centrifuged immediately after tapping. If pleural or ascitic fluid is allowed to stand for several hours in an ice box or at room temperature, partial sedimentation, associated with the formation of a scanty, diffuse, flocculent, fibrin network, occurs. This fibrin network may then be thrown down by centrifuging at high speed and firmly enmeshes the cellular elements of the fluid, holding them together during subsequent handling. Unfortunately, degenerative changes take place in the cellular elements of the fluid if it is allowed to stand too long. The interval between tapping and centrifuging must, therefore, represent a compromise between these two conflicting factors. We have found that most specimens of fluids develop sufficient fibrin network for a firm sediment after three to four hours. If kept in an ice box, the cellular changes during this period, as shown by comparison with fluids centrifuged immediately after tapping, are of no practical significance. Bloody fluids must be allowed to stand longer than nonbloody fluids, as the presence of much blood interferes with the obtaining of a firm nonfriable sediment.

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TABLE 1.—*Comparison of the Sediment Findings With the Final Clinical Diagnosis*

Type of Fluid	Totals	Positive		Per Cent of Correlation	Positive Clinical Diagnosis made by	
		Microscopically	Clinically		Operation	Autopsy
Ascitic	25	13	16	81.2%	8	8
Pleural	17	5	8	62.5%	0	8
Total	42	18	24	75.0%	8	16

The centrifuging must be done at the highest practical speed, over 3600 r. p. m. if possible. About five minutes at this speed is sufficient. Other conditions being equal, the higher the speed of centrifuging the firmer the resultant sediment. The clear supernatent fluid is then poured off without disturbing the sediment, the tube refilled with fresh fluid, and recentrifuged. This is repeated until a sufficiently large "button" of sediment is obtained.

The sediment should be left undisturbed in the centrifuge tube during fixation. Ten per cent formalin is very satisfactory although any other fixative may be used. After fixation the sediment is loosened by sliding a fine wire between it and the wall of the tube. The "button" of sediment then may be handled like an ordinary block of tissue during the subsequent processes of embedding and sectioning.

TABLE 2.—*Comparison of the Sediment Findings With the Type of Malignancy Present*

Type of Tumor	Fluid	No. of Cases	Tumor Cells Found in
Uterine adenocarcinoma	Ascitic	2	2
Papillary ovarian carcinoma	Ascitic	3	3
Carcinoma of the colon	Ascitic	3	1
Carcinoma of the stomach	Ascitic	1	1
Carcinoma of the breast	Ascitic Pleural	1 2	0 1
Primary carcinoma of the lung	Ascitic Pleural	1 3	1 2
Carcinomatosis (primary not determined)	Ascitic Pleural	5 3	5 2
Totals		24	18

Most fluids show little tendency toward macroscopic layering of the sediment. When blood is present, however, the red cells settle to the bottom while the mesothelial cells, lymphocytes, and polymorphonuclears form a top layer. Tumor cells, if present, may lie in any or all of these layers. The "button" of sediment is, therefore, split in

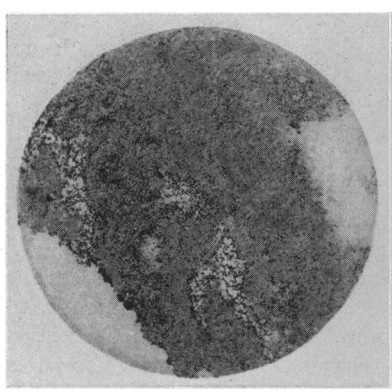

Fig. 1.—Pleural fluid. Cardiac decompensation. Masses of vacuolated mesothelial cells in diffuse sheets and clumps lie in a stroma composed of fibrin and coagulated protein. Lymphocytes, red blood cells, and occasional polymorphonuclears are present.

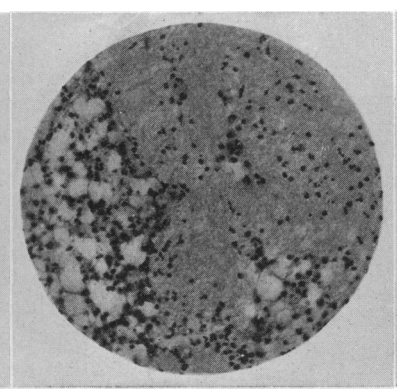

Fig. 2.—Pleural fluid. High power of Fig. 1. The sheet-like arrangement and uniformity of the mesothelial cells are quite characteristic.

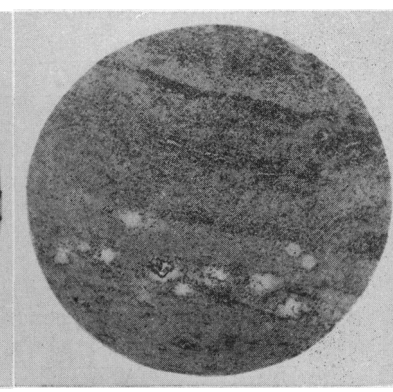

Fig. 3. Ascitic fluid. Carcinoma of the transverse colon. The clump of deep-staining, tumor cells stands out in sharp contrast to the lighter staining, more uniform mesothelial cells adjacent to it. The nuclei of the tumor cells are larger, and the cells vary in size and shape. Vacuolization is also present.

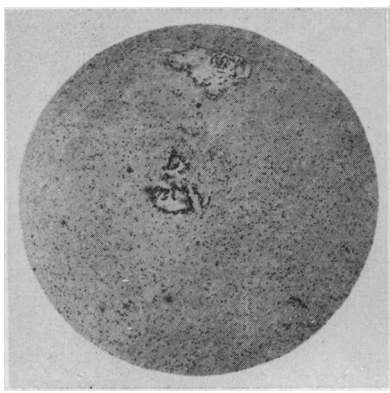

Fig. 4.—Ascitic fluid. Carcinomatosis. The tumor cells are definitely clumped, larger, and deeper staining than the other cells in the sediment.

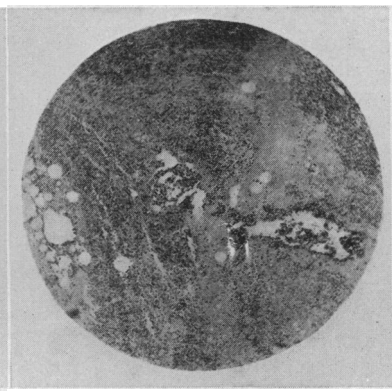

Fig. 5.—Ascitic fluid. Carcinoma of the ovary.

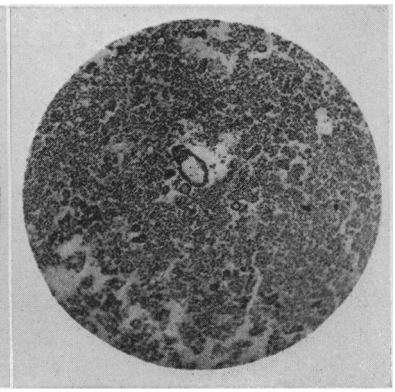

Fig. 6.—Carcinoma of the ovary. Nearly every cell in the field is of neoplastic origin. Although the isolated cells show polymorphism, mitotic figures, and occasional multinucleation, they would justify only a tentative diagnosis of malignancy. There are also clumps of similar cells with an alveolar arrangement. The definite diagnosis of malignancy depends upon these clumps.

two from above downward after embedding and the sections cut to include all these layers.

The cellular elements found in transudates and exudates of nonmalignant origin vary in number and type according to the etiology of the effusion. Lymphocytes predominate in tuberculous and polymorphonuclear leukocytes in nontuberculous infections. In mechanical effusions, mesothelial cells, either singly or in sheets or groups, are present in large numbers. These cells are mononuclear and vary little in size and shape. When grouped about fragments of fibrin or coagulated protein, they may simulate, at first sight, the appearance of a papillary type of malignancy. Pleural effusions caused by either tuberculosis or malignancy may contain numerous red blood cells.

Effusion associated with malignancy, involving the peritoneum or pleura, frequently contain tumor cells and occasionally even small fragments of neoplastic tissue in which may be recognized the relations of the tumor cells to their stroma. Fluids containing tissue fragments or groups of tumor cells offer little difficulty and ordinarily permit a positive diagnosis of malignancy. The cells of these clumps usually are larger than the other non-neoplastic cells of the sediment and because of their deeper staining give the slide a mottled appearance even under the low powers of the microscope. Frequently these clumps show a papillary or alveolar arrangement of the cells. Other fluids may contain a preponderance of isolated cells without any pattern formation. These offer the greatest difficulty in diagnosis, and, if no definite clumps are found, usually permit only a tentative diagnosis of malignancy. The differentiation of neoplastic cells from mesothelial cells in such sediments is based on marked variation in size and shape, or the presence of large numbers of unusual-appearing cells, as well as on cytological factors such as multinucleation, giant nuclei, and the presence of mitotic figures. Vacuolization of the cytoplasm is more common in tumor cells, but is also seen in the mesothelial cells of long standing effusions.

The results of the examination of the pleural or ascitic fluids from forty-two cases are given in Table 1. As very few specimens of fluid were

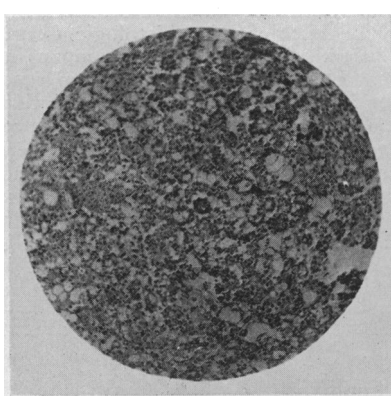

Fig. 7.—Ascitic fluid. Adenocarcinoma of the uterus. Most of the tumor cells are grouped in clumps and rosettes. A giant multinucleated tumor cell lies near the center of the field.

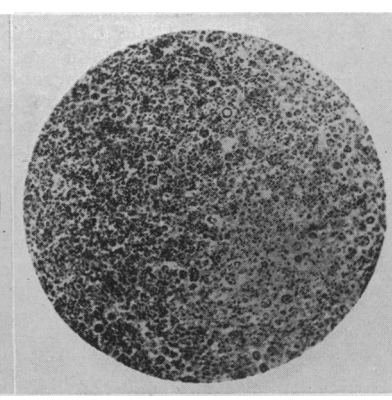

Fig. 8.—Pleural fluid. Primary carcinoma of the lung. Masses of tumor cells are arranged in clumps, rosettes, and pseudo-alveoli. Many of the cells have a vacuolated cytoplasm. Mitotic figures are numerous.

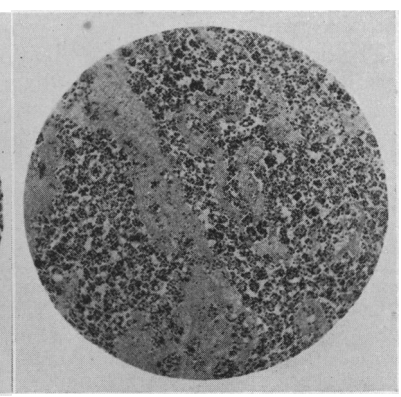

Fig. 9.—Pleural fluid. Primary carcinoma of the lung.

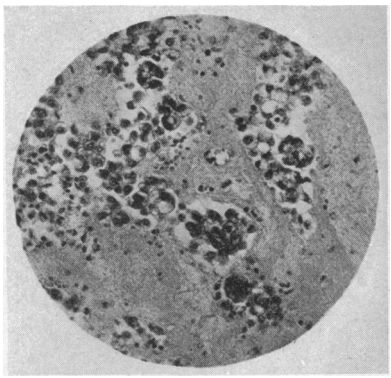

Fig. 10. — Pleural fluid. Primary carcinoma of the lung. A high power of Fig. 9. The polymorphism, deep staining, and vacuolization of the tumor cells are well shown.

sent to the laboratory from patients with proven cirrhosis of the liver or cardiac decompensation, the series shows a definite preponderance of cases clinically suspected of malignancy.

Twenty-four cases were proved malignant either by operation (exploratory or biopsy) or by autopsy. In eighteen of these, tumor cells were recognized in the sectionized sediment of the centrifuged ascitic or pleural fluids. Table 2 lists the type of malignancy in these cases.

The percentage of positive findings is high when the effusions are the result of malignant involvement of the pleura or peritoneum. In our series over 80 per cent of the specimens of ascitic fluid and over 60 per cent of the specimens of pleural fluid from such cases showed positive findings. These positive findings are quite accurate, and considerable reliance may be placed upon them in establishing the diagnosis and prognosis. On the other hand, a negative report does not rule out malignancy and is of no more significance than a negative report on any other laboratory procedure.

CONCLUSIONS

1. The examination of the sectioned centrifuged sediment of ascitic and pleural fluids is a valuable aid in the diagnosis of intra-abdominal or intrathoracic malignancy.

2. A positive diagnosis should be made only on the basis of definite fragments or groups of recognizable tumor cells. Isolated cells, regardless of appearance or the presence or absence of mitotic figures, justify no more than a diagnosis of probable malignancy.

The accuracy of these examinations is high and permits a positive or probable diagnosis of malignancy in about 70 per cent of the effusions caused by malignant involvement of the pleura or the peritoneum.

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PERIARTERITIS NODOSA WITH REMISSION OF SYMPTOMS*

REPORT OF CASE

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PERIARTERITIS nodosa is the pathologically descriptive name given by Kussmaul and Maier [1] in 1866 to a disease of the small arteries. A number of excellent summaries by Lamb,[2] Ophüls,[3] and Singer [4] have appeared in the medical literature. Singer [4] brought the total of reported cases to 130. Since then thirteen new cases have been added. Less than twenty of the total cases have been reported in our American medical literature, partly, no doubt, because of the lack of routine histologic autopsy studies. In this country about 12 per cent of the cases have been diagnosed before autopsy through biopsy studies of skin lesions or tissue removed at operation.

The following case report is presented not only in the hope of stimulating interest in the etiology and diagnosis of periarteritis nodosa, but because of its favorable response to arsenical treatment.

REPORT OF CASE

M. N., age forty-one. Barber. On September 17, 1930, he came because of "lumps all over body." Family history negative. Personal history negative. Three weeks before, he developed "lumps over the body." He had to give up his work, also his drum corps work because of pain when handling the sticks. For the past several weeks he has had severe pains in the hands, arms, and legs. Of late these pains have been sufficiently severe so that it was impossible for him to shake hands, difficult to walk, and almost impossible to sleep. Two or three new skin lesions appeared every day.

Examination.—Eyes negative. Blood pressure, 130/82. Pulse 76. Nose: Septum deviated to the left. Tonsils septic. Heart, lungs, and abdomen negative. Skin: Over the extensor surface of the forearms and on the legs there were small, hard, movable nodules about the size of shot. He also had three subcutaneous lesions on the face. Wassermann negative. Urine showed pus cells, a few coarse granular and small granular casts, with an occasional hyaline cast.

A biopsy specimen was sent to Dr. A. S. Warthin at the University of Michigan for histologic examination and he has kindly sent the accompanying microphotographs. I am also indebted to Doctor Warthin for the following pathologic description: "The blood vessels (arteries) present the appearances of an advanced second or inflammatory stage of periarteritis nodosa in the form of a marked polymorphonuclear infiltration of media and adventitia, and extending through the perivascular lymphatics. There are areas of localized necrosis of the vessel walls, with destruction of the intima and inner media, in some places extending entirely through the vessel walls. Associated with the cellular infiltration there is a fibrinous exudate in the form of fibrin threads. In some areas there is a reactive proliferation of the intima, and an organizing thrombus in the lumen. Some vessels are completely obturated by the thrombus. Some of the smaller arterioles show a later stage

* Read before the joint meeting of Pathology and Bacteriology and General Medicine Sections of the California Medical Association at the sixtieth annual session, San Francisco, April 27-30, 1931.